Sulfonium Salts. VII. Halogenation of Thiophane. Studies on the Mechanism of the Pummerer Reaction[1]

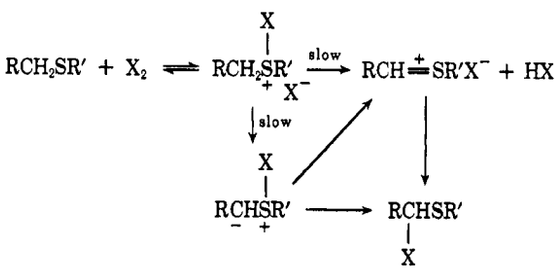
G. EDWIN WILSON, JR.,* AND RICHARD ALBERT[2]

Department of Chemistry, Polytechnic Institute of Brooklyn, Brooklyn, New York 11201

Received February 21, 1973

The effects of solvent and added reagents on the product distributions for the chlorination and bromination of thiophane were examined. Addition of common acid or triethylamine leads to an increase in the ratio of 2-halothiophane, but trifluoroacetic acid, *p*-toluenesulfonic acid, and boron trifluoride lead to an increase in the amount of 2,3-dihalothiophane. Competitive kinetic isotope effects of 5.1 and 3.6 were measured for chlorination and bromination, respectively.

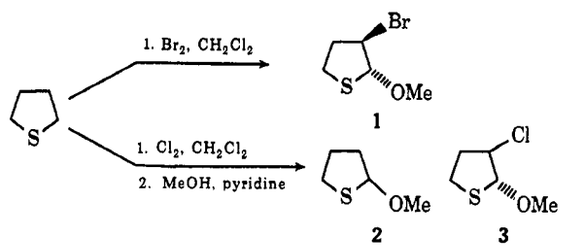
The Pummerer reaction of halosulfonium salts formed by halogenation of sulfides has received considerable attention because of its mechanistic subtleties and its utility in synthetic schemes.[3] The possible series of steps generally considered to be involved in this reaction is shown below.



Recent work[4] has established that the complex of bromine with thiophane in the solid state is a greatly distorted charge-transfer complex, probably with a high degree of ionic character. By contrast, the complex of chlorine with bis-*p*-chlorophenyl sulfide adopts a trigonal bipyramidal structure in the solid state.[5] In solution complexation of bis-*p*-fluorophenyl sulfide with chlorine is rapidly reversible between a seemingly covalent complex and starting materials.[6] Thus true halosulfonium salts may be present in very small concentrations.

The nature of the transformation of the halosulfonium salt to the α-halo sulfide is not yet completely resolved. Both a concerted process involving a sulfocarbonium ion[7] and a stepwise procedure through an ylide[8,9] have been proposed. Recent evidence suggests that the reactive species in *N*-chlorosuccinimide reactions may be a succinimidyl sulfonium salt[10] rather than a chlorosulfonium salt, as previously supposed.[9] Although it has been clear for some time that a sulfocarbonium ion may exist as a reaction intermediate, no firm proof for this species has been reported.

Bromination of thiophane in methylene chloride followed by treatment with methanol and pyridine leads to *trans*-3-bromo-2-methoxythiophane (**1**) and recovered thiophane in equimolar quantities.[2] Similarly, treatment of thiophane with chlorine followed by methanolysis led to both the normal Pummerer rearrangement product, 2-methoxythiophane (**2**), and *trans*-3-chloro-2-methoxythiophane (**3**) in a ratio of 2.4:1, as well as recovered thiophane.[2] Here we report studies concerning the effects of solvents and added reagents on the halogenation reactions which establish the presence of a sulfocarbonium ion intermediate in the Pummerer rearrangement of a halosulfonium salt.



Results

Solvent and Other Medium Effects on the Halogenation Reaction.—The chlorination of thiophane conducted in CCl_4 and followed by methanolysis produced two products, 2-methoxythiophane and 3-chloro-2-methoxythiophane, in a ratio ($\alpha/\alpha,\beta$) of 18.3. Chlorination in methylene chloride gave a ratio of 2.4. In each case chlorine was added at 0–5°, after which the temperature was raised to 40° and maintained there until hydrogen halide evolution was complete. The results in a series of solvents are shown in Table I.

TABLE I

EFFECT OF SOLVENTS ON THE PRODUCT RATIO FOR THE CHLORINATION OF THIOPHANE[a] AT 40°

Solvent	$\alpha/\alpha,\beta$[b]	Solvent	$\alpha/\alpha,\beta$[b]
CCl_4	18.3	$PhNO_2$	1.4
CH_2Cl_2	2.5	PhH	14.5
SO_2[c]	0.12	CH_3CN	0.50
CH_3NO_2	0.51		

[a] Initial thiophane concentration was 0.76 mol/l. [b] Molar ratio of α-methoxythiophane to α-methoxy-β-chlorothiophane. [c] Run at −15°.

Generally, the more polar the solvent the smaller the ratio of 2-substituted to disubstituted material ($\alpha/\alpha,\beta$); however, there were several inconsistencies with this in-

(1) Previous paper: G. E. Wilson, Jr., and R. Albert, *J. Org. Chem.*, **38**, 2156 (1973).

(2) Taken from the dissertation of Richard Albert, submitted to the Polytechnic Institute of Brooklyn in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry.

(3) For a review of the Pummerer reaction, see G. A. Russell and G. J. Mikol in B. S. Thyagarajan, Ed., "Mechanisms of Molecular Migrations," Vol. 1, Wiley, New York, N. Y., 1968, p 157.

(4) G. Allegra, G. E. Wilson, Jr., C. Pedone, E. Benedetti, and R. Albert, *J. Amer. Chem. Soc.*, **92**, 4002 (1970).

(5) N. C. Baenzinger, R. E. Buckles, Jr., R. J. Maner, and T. D. Simpson, *J. Amer. Chem. Soc.*, **91**, 5749 (1969).

(6) G. E. Wilson, Jr., and M. M. Y. Chang, *Tetrahedron Lett.*, 875 (1971).

(7) For lead references, see G. E. Wilson, Jr., and M. G. Huang, *J. Org. Chem.*, **35**, 3002 (1970).

(8) F. G. Bordwell and B. M. Pitt, *J. Amer. Chem. Soc.*, **77**, 572 (1955).

(9) D. L. Tuleen and T. B. Stephens, *J. Org. Chem.*, **34**, 31 (1969), and references cited therein.

(10) E. Vilsmaier and W. Sprugel, *Justus Liebigs Ann. Chem.*, **747**, 151 (1971).

verse dependency on polarity. Nitromethane and nitrobenzene have dielectric constants of 39.4 and 36.1, respectively, but gave product ratios of 0.51 and 1.4, respectively. Acetonitrile, with a dielectric constant of 38.8, gave a product ratio of 0.50.

Chlorination conducted in CCl_4 with 10% boron trifluoride changed the ratio $\alpha/\alpha,\beta$ from 18.3 to 0.21. Trifluoroacetic and *p*-toluenesulfonic acid reduced the product ratio to 0.31 and 0.25, respectively. Addition of triethylamine to a methylene chloride solution of bromothiophanium bromide led to 2-bromothiophane. Addition of lutidinium chloride to the chlorination mixture led to the formation of only α-chlorothiophane. Lithium perchlorate acted in a fashion imitating a special salt effect; a solution 6.2×10^{-3} *M* in lithium perchlorate and 0.37 *M* in thiophane increased the ratio $\alpha/\alpha,\beta$ from 2.5 to 5.0. In contrast to the observation with benzyl sulfide,[7] the ratio $\alpha/\alpha,\beta$ is insensitive to initial concentration of reagents, not varying by more than 40% as the concentration of thiophane and halogen was varied by 600%. These results are displayed in Tables II and III.

TABLE II

REAGENT EFFECTS ON THE HALOGENATION OF THIOPHANE[a]

Reagent	Concn, mol/l.	$\alpha/\alpha,\beta$
None added		2.5
Hydrogen chloride	0.88	>80
	1.3	>80
	2.6	>80
Lutidinium chloride	0.53	>80
Hydrogen bromide[b]	0.0	0.09
	1.1	0.18
Trifluoroacetic acid	0.76	0.3
p-Toluenesulfonic acid	0.13	0.3
Triethylamine[b]	0.80	80
Sulfuryl chloride	0.76	0.3
Boron trifluoride	0.80	0.2

[a] The concentrations of thiophane and halogen were 0.38 mol/l. [b] Refers to the bromination of thiophane.

TABLE III

EFFECT OF INITIAL CONCENTRATION OF HALOGEN AND THIOPHANE IN METHYLENE CHLORIDE ON THE PRODUCT RATIO $\alpha/\alpha,\beta$

Concn, mol/l.		
Thiophane	Chlorine	$\alpha/\alpha,\beta$[a]
0.19	0.19	2.3
0.38	0.38	2.6
0.75	0.75	1.6
1.14	1.14	1.8

[a] Molar ratio of α-methoxythiophane to α-methoxy-, chlorothiophane.

Kinetic Isotope Effects.—Competitive hydrogen–deuterium kinetic isotope effects were measured for both the chlorination and bromination reactions in carbon tetrachloride and chloroform, using 2,2-dideuteriothiophane. The deuterated thiophane was obtained by lithium aluminum deuteride reduction of γ-butyrolactone to 1,1-dideuterio-1,4-butanediol, conversion to 1,1-dideuterio-1,4-dichlorobutane using thionyl chloride, and cyclization to the desired compound with sodium sulfide in ethanol. The kinetic isotope effect for chlorination in carbon tetrachloride ($k_H/k_D = 5.1$) in which there was less than 5% of **3** could be obtained by nmr methods in the following manner. The area of the methine signal (A_1) is proportional to the number of moles of α-chlorothiophane formed by proton removal. The area of the upfield multiplet (A_2) is proportional to four times the molar concentration of 2-chlorothiophane formed by proton removal plus six times the molar concentration of 2-chlorothiophane formed by deuterium removal. Thus k_H/k_D is given by

$$k_H/k_D = \frac{6A_1}{A_2 - 4A_1}$$

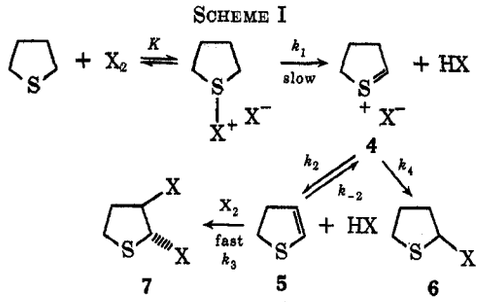
The isotope effect for the bromination reaction (3.6) is easily obtained by nmr because the two methine absorptions are separated from each other. Thus, the area of the downfield absorption (A_1), due to the 2 proton of 2,3-dibromothiophane, represents the rate of proton removal. The upfield methine absorption (A_2) is common to both products. Thus,

$$k_H/k_D = \frac{A_1}{A_2 - A_1}$$

Discussion

The reagent and solvent effects on the halogenations of thiophane are all consistent with the series of steps shown in Scheme I.

SCHEME I



In this scheme the initial equilibrium is considered to be fast and proton removal is considered rate limiting. The relative magnitudes of k_2, k_{-2}, k_3, and k_4 are important in determining the partitioning of the products. Thus, a preponderance of **7** in the case of bromination of thiophane could occur because $k_4 < k_3$ or because $k_2 > k_{-2}$. If formation of **6** were reversible, the reaction would drain into **7** until the supply of the necessary halogenating agent was depleted. That this was not the case was demonstrated for both 2-bromo- and 2-chlorothiophane, which were stable under the reaction conditions in the absence of halogenating agent.

Some solvent sensitivity would be expected for the equilibrium **4** ⇌ **5**, but not enough to account for the observed dramatic reversal in the favored product when changing from carbon tetrachloride to sulfur dioxide. Thus, changes in the relative magnitudes of k_2 and k_{-2} cannot be used to explain the results.

When $k_3 > k_4$, the product ratio reflects the difference between the activation energies for proton loss from the sulfocarbonium ion **4** and attack by anion at the α-carbon atom.

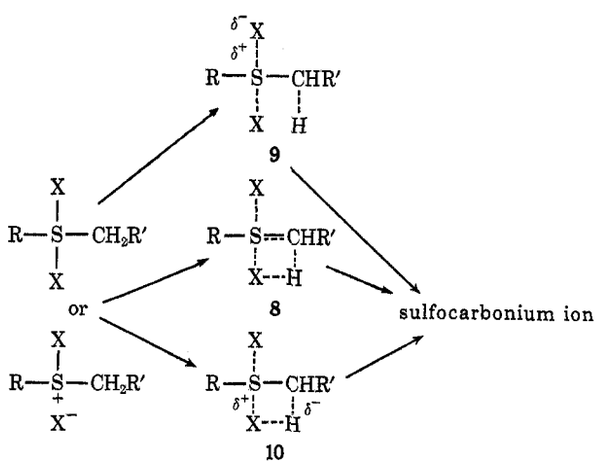
The relative magnitudes of the activation energies for formation of **5** and **6** from **4** can be rationalized in

terms of the hard and soft acid and base theory developed by Pearson[11a] and Klopman.[11b] Klopman[11b] has shown theoretically that, as the solvent becomes more polar, hydrogen chloride ionizes more, becoming a stronger acid. The proton becomes harder, the chloride ion becomes softer, and the bond between them becomes weaker. Thus, the energy of the transition state for olefin protonation by hydrogen chloride, and also the energy of the transition state for deprotonation of the sulfocarbonium ion **4**, decreases with increased solvent polarity. By contrast, attack of chloride ion at the relatively hard carbonium carbon atom of **4** should become less favorable as the solvent is made more polar. Both of these effects operate in the direction to reduce the ratio $\alpha/\alpha,\beta$, which is consistent with the observations.

Addition of the common acid has the expected dramatic effect of increasing the proportion of **4** by shifting the equilibrium **4** $\rightleftharpoons$ **5** toward **4**. The effect of lutidinium chloride may be quite similar with the lutidinium ion supplying the proton.

That $\alpha/\alpha,\beta$ drops with addition of trifluoroacetic acid, *p*-toluenesulfonic acid, and boron trifluoride etherate may be due to a reduction of the nucleophilic activity of the chloride ion caused by complexation, in the first two cases by the proton and in the last case by the boron trifluoride. Even the weak bases in solution, however, can act as proton acceptors for the conversion of **4** to **5**.

The data now available in this and other systems permit, we believe, a detailed picture for the removal of the α proton in the generalized Pummerer reaction. In this transformation, which may best be described in the terminology of Ko and Parker[12] as an E2S elimination, the transition state for this postulated mechanism (**8**) involves weak bonding between the nucleophile–base and both the sulfur atom and the α-hydrogen atom and synchronous weakening of the remaining sulfur–leaving group bond. This transition state may also be looked at as the central transition state in the variable E2 transition-state theory[13,14] as applied to C–S double bond formation. For this modified theory the reference central transition state (**8**) possesses geometry similar to the sulfurane and is one in which bond breaking of the two S–X bonds is about equal. The E1 extreme (**9**) involves cleavage of the S–X bond preceding H–X loss. Finally, the E1cB extreme (**10**) involves loss of HX proceeding ahead of S–X cleavage to provide an ylide-like transition state.



It is clear that any of these transition states may be arrived at from either a sulfurane or a sulfonium salt, both of which have been shown to be possible structures for formalized sulfonium salts in the solid state[5,15,16] and in the solution.[6,17]

In analogy with carbon systems, one would expect that, in symmetric systems with the nucleophile–base structurally identical with the leaving group on sulfur, exchange of the electronegative ligand might be faster than proton removal and that reprotonation of a sulfocarbonium ion intermediate would be an unfavorable step because of the necessity for a termolecular collision. In fact, it is clear from work with "halosulfonium salts"[6] and alkoxysulfonium salts[18] that, for those compounds which do not exist as the sulfurane, displacement of the electronegative ligand from the sulfonium sulfur atom by an anionic nucleophile can occur more rapidly than the Pummerer reaction. For acetoxysulfonium salts, however, it has been shown that the rate of the Pummerer reaction of aryl methyl sulfoxides is greater than the rate of oxygen exchange.[19] Finally, we[7,20] and others[21–23] have been unable to demonstrate significant exchange of the α proton accompanying the Pummerer reaction.

For the E2S mechanisms, one would predict that weakly basic anions which allow bonding to sulfur through a strongly electron-withdrawing atom will be characterized by relatively central transition states. However, strongly basic anions might show a preference for attack at the proton leading to an ylide.

The relatively central transition state should be accompanied by a high kinetic isotope effect, and transition states at either extreme should give isotope effects tending toward unity. The observed isotope effects for the halogenations of thiophane eliminate an E1cB mechanism; all variations of such a mechanism require that k_H/k_D be equal to unity.[24] The observation that the value for the competitive isotope effect of the chlorosulfonium salt is higher than that of the bromosulfonium salt is readily explained in terms of the proposed mechanism using the theory of hard and soft acids and bases. The sulfur atom of a sulfonium salt should be moderately hard in analogy with the sulfur atom in sulfinyl and sulfonyl derivatives.[25] Thus, one would expect relatively stronger bonding between sulfur and chlorine than between sulfur and bromine in the transition state. Similarly, the chlorine should develop bonding with hydrogen more easily than

(11) (a) R. G. Pearson and J. Songstad, *J. Amer. Chem. Soc.*, **89**, 1827 (1967); (b) G. Klopman, *ibid.*, **90**, 223 (1968).
(12) E. C. F. Ko and A. J. Parker, *J. Amer. Chem. Soc.*, **90**, 6447 (1968).
(13) J. F. Bunnett, *Angew. Chem., Int. Ed. Engl.*, **1**, 225 (1962).
(14) R. A. Bartsch and J. F. Bunnett, *J. Amer. Chem. Soc.*, **91**, 1376 (1969).
(15) I. Kapovitz and A. Kalman, *Chem. Commun.*, 649 (1971).
(16) I. C. Paul, J. C. Martin, and E. F. Perazzi, *J. Amer. Chem. Soc.*, **93**, 6674 (1971).
(17) W. A. Sheppard, *J. Amer. Chem. Soc.*, **93**, 5597 (1971).
(18) C. R. Johnson and W. G. Phillips, *Tetrahedron Lett.*, 2101 (1965).
(19) S. Oae and M. Kise, *Tetrahedron Lett.*, 2261 (1968).
(20) G. E. Wilson, Jr., and C. J. Strong, *J. Org. Chem.*, **37**, 2376 (1972).
(21) C. R. Johnson and W. G. Phillips, *J. Org. Chem.*, **32**, 1926 (1967).
(22) C. R. Johnson, J. C. Sharp, and W. G. Phillips, *Tetrahedron Lett.*, 5299 (1967).
(23) W. G. Phillips and K. W. Ratts, *J. Org. Chem.*, **36**, 3145 (1971).
(24) W. K. Kwok, W. G. Lee, and S. I. Miller, *J. Amer. Chem. Soc.*, **91**, 468 (1969); Z. Rappoport, *Tetrahedron Lett.*, 3401 (1968).
(25) J. L. Kice and G. B. Large, *J. Amer. Chem. Soc.*, **90**, 4076 (1968); J. L. Kice and G. Guaraldi, *Tetrahedron Lett.*, 6135 (1966).

should the bromine. Thus the bromination reaction would be expected to tend toward the E1 extreme transition state, **9**. For acetoxysulfonium salts, because of the hardness of the oxygen atoms, one would expect the transition state to be relatively more central than that for the bromosulfonium salt, and, indeed, the reaction of dibenzyl sulfoxide with acetic anhydride provided a high competitive hydrogen kinetic isotope effect.[21] Finally, it is clear that the relative magnitudes of the isotope effects are not a function of the geometrical constraint imposed by the thiophane ring, for a similar order was observed with benzyl sulfide.[7]

Where other factors are equal, a preference for removal of the most acidic proton might be expected for the Pummerer reaction. The reaction, however, should be highly sensitive to steric effects as the size of the anion–base increases if coplanarity of the proton, the leaving group, and the nucleophile–base is required. This would agree with the observed preference methyl < ethyl ≈ *n*-propyl < isopropyl observed by Tuleen and coworkers[26] for the *N*-chlorosuccinimide reaction, assuming chloride ion to be the anion, and with the order methyl > *n*-propyl, isopropyl, *n*-butyl observed by Johnson and coworkers[22] for acetic anhydride reactions with sulfoxides.

Finally, it is clear that the E2S mechanism also is in accord with observations of racemization and reduction of sulfoxides by hydrogen halides in aqueous solutions[27] where the activity of the anion is reduced by coordination to water so that there is little tendency to remove the α proton from the sulfonium salt intermediate.

Experimental Section

1,1-Dideuterio-1,4-dichlorobutane.—To a solution of 8.0 g (0.087 mol) of 1,1-dideuterio-1,4-dihydroxybutane in 50 ml of benzene was slowly added with stirring 25.0 g (0.21 mol) of thionyl chloride in 30 ml of benzene at such a rate that the temperature remained between 25 and 30°. After complete addition of the thionyl chloride, the solution was stirred at ambient temperature for 12 hr, then the solvent was removed on the rotary evaporator, and the residue was distilled, bp 35° (1.8 mm), providing 8.7 g (79% yield) of 1,1-dideuterio-1,4-dichlorobutane, nmr ($DCCl_3$) τ 6.01 (m, 2 H) and 8.19 (m, 4 H).

α,α-Dideuteriothiophane.—To 100 ml of refluxing dimethylformamide was added simultaneously a solution of 25 g (0.105 mol) of sodium sulfide nonahydrate in 40 ml of hot water and a solution of 8.7 g (0.07 mol) of 1,1-dideuterio-1,4-dichlorobutane in 20 ml of dimethylformamide at such a rate that gentle reflux was maintained. After addition of the reagents was completed, the system was heated under reflux for an additional 6 hr, and then 50 ml of the solution was removed by distillation. The aqueous distillate was made alkaline with 4.0 g (0.10 mol) of solid sodium hydroxide and brought to saturation with sodium chloride, after which the organic layer was separated, dried, and distilled through a 15-cm Vigreux column, bp 110° (760 mm), giving 3.5 g (57% yield) of α,α-dideuteriothiophane: ir λ_{max}^{neat} 2948, 2863, 2213, 2138, 1681, 1439 cm^{-1}; nmr (CCl_4) τ 7.30 (m, 2 H) and 8.14 (m, 4 H).

Solvent Effects on the Halogenation of Thiophane.—To a solution of 2.5 g (0.028 mol) of thiophane in 75 ml of solvent was added in a nitrogen carrier 2.0 g (0.62 ml, 0.028 mol) of chlorine with stirring and while maintaining the temperature between 5 and 10°. After chlorine addition was complete, the temperature was rapidly raised to 40°, and stirring was continued until all hydrogen chloride evolution ceased. Then the solution was cooled and charged with 1.0 g (0.031 mol) of methanol and 2.2 g (0.03 mol) of pyridine in small portions, and stirring was continued overnight. The crude reaction mixture was analyzed on the vpc. Components were identified by mixed injections with authentic samples on SE-30 and FFAP columns. The mole percentage of thiophane, α-methoxythiophane, and α-methoxy-β-chlorothiophane were averaged over three to five runs and two to three injections per run. The vpc columns employed were a 9 ft × 0.25 in. aluminum column packed with 15% SE-30 on 60/80 mesh Chromosorb P and a 6 ft × 0.25 in. steel column packed with 20% FFAP on 60/80 mesh Chromosorb W.

Reagent Effects on the Halogenation of Thiophane.—To a solution of 2.5 g (0.028 mol) of thiophane and one of the following [5.7 g (0.04 mol) of lutidinium chloride, 7.65 g (0.0567 mol) of sulfuryl chloride, 50 mg (4.7×10^{-4} mol) of lithium perchlorate, 1.74 g (0.010 mol) of boron trifluoride, or 0.24, 0.48, or 0.72 g (0.066, 0.098, or 0.196 mol) of hydrogen chloride] in 75 ml of methylene chloride was added in a nitrogen carrier 2.0 g (0.028 mol) of chlorine with stirring while the temperature was maintained between 5 and 10°. The hydrogen chloride run was allowed to reflux under a Dry Ice trap sealed with an inflatable balloon. After chlorine addition was complete, the temperature was rapidly raised to 40°, and stirring was continued until all hydrogen chloride evolution had ceased. The solution was cooled, charged with 1.0 g (0.031 mol) of methanol and then with 2.2 g (0.03 mol) of pyridine in small portions, and stirring was continued overnight. Work-up and analysis were as above.

Effect of Hydrogen Bromide on the Bromination of Thiophane.—To a solution of 2.5 g (0.028 mol) of thiophane and 0.082 mol of hydrogen bromide in 75 ml of methylene chlorine was added 2.0 g (0.028 mol) of bromine with stirring while the temperature was maintained between 5 and 10°. Hydrogen bromide was refluxed under a liquid nitrogen trap which was closed by an inflatable balloon. After bromine addition was complete, the temperature was rapidly raised to 40°, and stirring was continued overnight. The solution was cooled and charged with 1.0 g (0.031 mol) of methanol and then with 2.2 g (0.03 mol) of pyridine in small portions, and stirring was continued overnight. The crude reaction mixture was analyzed on the vpc as above.

Kinetic Isotope Study.—To 88 mg (1 mmol) of α,α-dideuteriothiophane was added 0.80 ml of 1.25 *N* chlorine in deuteriochloroform at 40°. When the reaction was complete, the absorptions 4.15 and 7.12 ppm downfield from TMS were scanned at 100 and 500 cps sweep widths using a Varian Associates Model A-60 spectrometer. Averaging the area integration over five passes yielded the product isotopic ratio. A similar procedure was employed for the bromination of thiophane-d_2 except that the resonance peaks examined were 4.03 and 4.88 ppm downfield from TMS.

α-Acetoxythiophane.—Tetramethylene sulfoxide (16.7 g, 0.160 mol) and 16.6 g (0.160 mol) of acetic anhydride in 50 ml of benzene were heated under reflux under nitrogen for 4 hr, then allowed to cool to room temperature. The solution was washed with 5% aqueous sodium bicarbonate until the aqueous layer was no longer acidic. The organic layer was dried over sodium sulfate, the solvent was removed on a rotary evaporator, and the 14.6 g of residue was distilled, bp 47° (0.4 mm), giving 12.0 g (51% yield) of α-acetoxythiophane: $n^{25}D$ 1.4896; ir ν_{max}^{neat} 2996 (CH), 2910 (CH), 1732 (C=O), 1200 (CO), and 912 cm^{-1}; nmr (CCl_4) τ 3.85 (1 H, m), 7.09 (2 H, m), 7.90 (4 H, m), and 7.97 (3 H, s).

Anal. Calcd for $C_6H_{10}O_2S$: C, 49.29; H, 6.90; S, 21.93; mol wt, 146.20. Found: C, 49.07; H, 6.86; S, 21.89; mol wt, 146 (*m/e* 104, mass spectrum, $M^+ - CH_2CO$).

2-(2-Thiophanyl)-2,3-dihydrothiophene.—Tetramethylene sulfoxide (10.4 g, 0.10 mol) and 50 ml of acetic acid were heated under nitrogen at 100° overnight. The solution was diluted with 150 ml of methylene chloride and washed several times with 100-ml portions of water and several times with portions of aqueous 5% sodium bicarbonate until the aqueous layer was neutral. The organic layer was dried over sodium sulfate, and the solvent was removed by rotary evaporation, leaving 6.65 g (83% yield) of crude material, 2.0 g of which was purified by chromatography on 100 g of alumina (M. Woelm, Woelm neutral, activity grade I) in a column of 1.8 × 60.0 cm. The crude product was added neat and then eluted using benzene, thus providing 1.5 g of pure 2-(2-thiophanyl)-2,3-dihydrothiophene in 62% yield: ir ν_{max}^{neat} 3000 (C=CH), 2842 (CH), 1648 (C=C), 1445, 1253, and 841 cm^{-1}; nmr τ 4.00 (1 H, m), 5.17 (1 H, m), 6.97 (4 H, m), and 7.98 (6 H, m).

(26) D. L. Tuleen and T. B. Stephens, *J. Org. Chem.*, **34**, 31 (1969).

(27) See, for example, D. Landini, G. Modena, F. Montanari, and G. Scorrano, *J. Amer. Chem. Soc.*, **92**, 7168 (1970); R. A. Strecker and K. K. Andersen, *J. Org. Chem.*, **33**, 2234 (1968).

Anal. Calcd for $C_8H_{12}S_2$: C, 55.76; H, 7.02; S, 37.22; mol wt, 172.316. Found: C, 55.35; H, 6.72; S, 37.72; mol wt, 172 (mass spectrum, molecular ion).

Reaction of Tetramethylene Sulfoxide with Acetyl Bromide.—To a solution of 5.2 g (0.05 mol) of tetramethylene sulfoxide in 100 ml of carbon tetrachloride was added with stirring an equimolar quantity of acetyl bromide at 0°; 1-bromothiophanium bromide deposited out of solution and was identified by nmr spectrometry.

Reaction of Tetramethylene Sulfoxide with Acetyl Chloride.—To a solution of 5.2 g (0.05 mol) of tetramethylene sulfoxide in 100 ml of methylene chloride was added with stirring an equimolar quantity of acetyl chloride at ambient temperature. After addition of the acetyl chloride was complete, the temperature was raised and kept at 40–50° until all hydrogen chloride evolution ceased. Then 4 g (0.125 mol) of methanol was added followed by 7.0 g (0.09 mol) of pyridine in small portions, and the mixture was stirred overnight.

With acetyl bromide, when carbon tetrachloride was employed as the solvent, bromothiophanium bromide was deposited out of solution. Analysis by mixed injection of the crude reaction mixture was by vpc as previously described.

Registry No.—Thiophane, 110-01-0; 1,1-dideuterio-1,4-dichlorobutane, 39495-73-3; 1,1-dideuterio-1,4-dihydroxybutane, 39495-74-4; thionyl chloride, 7719-09-7; α,α-dideuteriothiophane, 39495-75-5; α-acetoxythiophane, 1608-66-8; tetramethylene sulfoxide, 1600-44-8; 2-(2-thiophanyl)-2,3-dihydrothiophene, 39495-77-7.

Acknowledgment.—We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for a grant in partial support of this work. A NASA graduate traineeship awarded to R. A. is gratefully acknowledged.

Quaternization of Thiazoles

G. B. BEHERA*

Postgraduate Department of Chemistry, Sambalpur University, Burla, Orissa, India

J. N. KAR, R. C. ACHARYA, AND M. K. ROUT

Mayurbhanj Chemical Laboratory, Ravenshaw College, Cuttack-3, Orissa, India

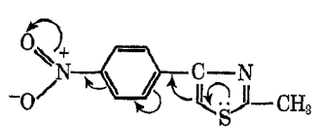
Received February 10, 1972

Different thiazoles have been prepared and their rate of quaternization with methyl iodide studied by the conductance method. The lower reactivity of quinaldine (**10**) over 2-methylbenzothiazole (**5**) has been explained on the basis of the β value of sulfur atom and the vinyl group. A charge transfer complex has been proposed to explain the rate retardation effect of an amino group, which otherwise should have accelerated the rate. The pK_a values of these thiazoles have been calculated by employing Edward's equation. The rate of quaternization in a series of isomeric alcohols has been investigated.

Quaternization has been a subject of interest since the days of Menschutkin.[1] The quaternization kinetics of heterocyclic bases like pyridine[2] and tetrahydroquinoline[3] have been investigated, but thiazoles have not been utilized for such studies. The quaternary salts of these thiazoles have been used by Rout, *et al.*,[4] for the synthesis of various dyes. The relative basicities of these thiazoles have been evaluated with the aid of Brooker's deviation factor.[5]

Results and Discussion

Thiazoles react with methyl iodide to form a quaternary salt. The rate data, Arrhenius parameters, and entropy of activation values are given in Table I. The reactivity of different 4-aryl substituted 2-methylthiazoles conform to the order **1** > **2** > **3** > **4**. This order of reactivity of different substituents is justifiable, since they oppose the main resonance of the sulfur atom with the thiazole ring[6] (I). The order of reactivity of other bases is **12** > **11** > **10** > **5** > **7** > **9** > **6** > **8**. The compounds **5**, **10**, and **11** belong to the same series of even alternant hydrocarbons. Quinaldine reacts more slowly than lepidine, possibly owing to the ortho effect. At 80°, the k values (extrapolated) are reversed, presumably owing to the loss of steric effect and the operation of the polar effects alone. Quinaldine reacts *ca.* four times slower than 2-methylbenzothiazole in agreement with the observation that the β value of sulfur is 25% lower than that of a vinyl group.[7]



I

The greater rate of reactivity of **1** over **8** is surprising, since an amino group would (1) increase the negative charge density around nitrogen in the reactant state and (2) stabilize the transition state. This decrease in rate may be due to the existence of an equilibrium between loose contact pairs and a charge trans-

(1) M. Menschutkin, *Z. Phys. Chem.*, **5**, 589 (1890).
(2) E. M. Kosower, *J. Amer. Chem. Soc.*, **80**, 3267 (1958).
(3) J. Wolford, G. Toth, G. Bernathi, and J. Kobor, *Tetrahedron Lett.*, **43**, 43, 4019 (1971).
(4) (a) P. K. Misra, B. K. Patnaik, and M. K. Rout, *J. Indian Chem. Soc.*, **36**, 35 (1959); (b) B. K. Sabata, B. K. Patnaik, and M. K. Rout, *ibid.*, **37**, 613 (1960); (c) K. Mukherjee, R. C. Parida, A. Nayak, and M. K. Rout, *ibid.*, **47**, 1121 (1970); (d) P. B. Tripathy and M. K. Rout, *J. Indian Chem. Soc.*, **39**, 103 (1962); (e) B. K. Sabata, B. K. Patnaik, and M. K. Rout, *ibid.*, **38**, 679 (1970); **47**, 1121 (1970); (f) D. C. Pati and M. K. Rout, *ibid.*, **45**, 425 (1968); (g) K. Mukherjee, C. S. Panda, S. Misra, G. B. Behera, and M. K. Rout, *ibid.*, **47**, 323 (1970).
(5) L. G. S. Brooker, S. G. De nt,D. W. Heseltine, and E. VanLare, *J. Amer. Chem. Soc.*, **75**, 4335 (1953).
(6) A. M. Acheson, "An Introduction to the Chemistry of Heterocyclic Compounds," The Queens College, Oxford, 1967.
(7) A. Streitweiser, Jr., "Molecular Orbital Theory for Organic Chemists," Wiley, New York, N. Y., 1962, p 127.